Abstracts

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Final Results of the Protected Superficial Femoral Artery Trial Using the Filter Wire EZ System

Muller-Hulsbeck S, Humme TH, Schafer JP, et al. Cardiovasc Intervent Radiol 2010;33:1120-7.

Conclusion: A distal protection device during femoral popliteal interventions reduces distal migration of debris.

Summary: The study evaluated the safety and efficacy of a single distal protection device (Filter Wire EZ Embolic Protection System, Boston Scientific, Mountain View, Calif) for capturing debris during superficial femoral artery (SFA) percutaneous interventions. An additional aim was to define the incidence of distal embolization during SFA interventions. This was a prospective, single-center registry. The study included 30 patients suitable for percutaneous transluminal angioplasty (PTA). Primary end points were occurrence of distal embolization, decreased runoff, improvement in ankle-brachial index (ABI), and number of filters containing emboli. Secondary end points included procedural or device-related death and/or clinical target lesion revascularization, device delivery, deployment success, and incidence of embolic recovery. Procedural success was defined as <30% residual stenosis, with no worsening of distal runoff as determined by angiography. The study enrolled 29 patients with 30 treated limbs, suitable for PTA, between February 2007 and March 2008. Claudication was the indication for intervention in 26 patients and critical limb ischemia in 3. One patient underwent treatment in both legs. The average degree of stenosis was 86% ± 7%, and stenosis length ranged from 8 to 88 mm. No procedural or device-related complications occurred. Average degree of residual stenosis was 10 % ± 10%. ABI improved from 0.56 ± 0.16 to 0.92 ± 0.19 ($P <$ .05). At 1 month, there was no ultrasound-detected waist stenoses or dissections. Microscopic debris was found in 27 of the 30 filters used. Particle size was 1200 ± 640 μm (range, 90-2000 μm). Histologic analysis indicated debris consisted of platelets, erythrocytes, inflammatory cells, extracellular matrix, and cholesterol. There was no correlation between lesion morphology and type of debris.

Comment: This is a small, single-center, nonrandomized commercially sponsored study with the first author having a consulting arrangement with the study sponsor. The study is obviously good marketing material for the manufacture of the FilterWire EZ System. However, assuming the author's observations are accurate, the study should bring some measure of concern to all who perform catheter-based SFA interventions, because these interventions seem to be nearly uniformly associated with distal embolization. Long-term clinical implications of these distal emboli remain to be defined, but as someone once said, they may not be bad, but they can't be good! The true clinical utility of embolic protection devices in all vascular beds remains an intriguing, and certainly a potentially profitable, avenue of research.

Pathogenesis of Acute Aortic Dissections: A Finite Element Stress Analysis

Nathan DP, Zu C, Gorman JH 3rd, et al. Ann Thorac Surg 2011;91: 458-64.

Conclusion: Wall stress in the thoracic aorta peaks above the sinotubular junction and distal to the left subclavian artery origin. Wall stress may contribute to the pathophysiology of thoracic aortic dissection.

Summary: In most cases, type A and type B thoracic aortic dissections originate with entry tears, respectively, above the sinotubular junction or distal to the left subclavian artery origin. Although thoracic dissection is influenced by many components, including aortic diameter, hypertension, and decreases in wall strength associated with Marfan syndrome or Ehlers-Danlos syndrome, the precise mechanistic rationale for origin of thoracic type A and type B dissections is not understood. The authors hypothesized that a biomechanical approach to predicting thoracic aortic walls stress may better define the risk of thoracic aortic dissection in individual patients. They mapped patterns of wall stress in the thoracic aorta in normal individuals, extrapolating wall stress patterns from normal individuals to those with potential dissection. They identified 47 patients whose thoracic aorta was normal by electrocardiogram-gated computed tomography angiography. The thoracic aorta was segmentally reconstructed and triangulated to create a geometric mesh with the ABAQUS/Explicit 6.3 program (HKS Inc, Pawtucket, RI). A systolic pressure load of 120 mm Hg was then used to construct a finite element analysis and to predict regional thoracic aortic wall stress. Local maximum wall stress was highest in the sinotubular junction in the ascending aorta and distal to the origins of the supra-aortic vessels, including the left subclavian artery, in the aortic arch. No errors of maximum wall stress were identified in the descending thoracic aorta. A comparison of areas of mean peak wall stress above the sinotubular junction (0.43 ± 0.77 MPa), distal to the left subclavian artery origin (0.021 ± 0.77 MPa), and in the descending thoracic aorta (0.06 ± 0.01 MPa) demonstrated significant levels of wall stress by aortic region ($P <$ .001).

Comment: The data indicate that there are peaks in wall stress in the normal thoracic aorta above the sinotubular junction and just distal to the origin of the left subclavian artery. The implication that peaks in wall stress may contribute to aortic dissection is a bit of "guilt by association." Preventing thoracic aortic dissection is likely to be a multifaceted task. Diameter, according to Laplace's Law, is currently used as a noninvasive surrogate of aortic wall stress. Surgical intervention is timed to occur before wall stress exceeds the maximal tensile strength of the aorta, estimated at about 800 kPs. Although the risk of acute aortic events is currently correlated roughly with size, even small aortas can have fatal dissections and ruptures. Improving wall strength of the aorta, decreasing expansion rates, and calculations of wall sheer stress will all likely, in the future, be used in the management of patients with thoracic and abdominal aortic disease.

Results of Single- and Two-Vessel Mesenteric Artery Stents for Chronic Mesenteric Ischemia

Malgor RD, Oderich GS, McKusick MA, et al. Ann Vasc Surg 2010;24: 1094-101.

Conclusions: Stenting of both the celiac artery and the superior mesenteric artery (SMA) for chronic mesenteric ischemia (CMI) does not reduce recurrent symptoms or reinterventions compared with stenting of the SMA alone. Isolated celiac stenting carries a high risk of symptom recurrence.

Summary: Mesenteric artery stenting is gaining wider acceptance for the treatment of CMI. It relieves symptoms of CMI in 78% to 100% and has lower morbidity and mortality compared with open reconstruction. However, the durability of mesenteric stenting is questioned. Primary patencies have ranged from 30% to 82%, and 17% to 64% of patients have recurrent symptoms at 2 years of follow-up (Atkins MD et al [J Vasc Surg 2007;45: 1162-71]; AbuRahma AF et al [J Endovasc Ther 2003;10:1046-53]). It is generally agreed that the SMA is the primary target vessel for revascularization for patients with CMI. In open surgical procedures, it is debated whether revascularization of the SMA alone is adequate treatment. In endovascular therapy for CMI, it is also unclear whether stenting of the celiac artery in addition to the SMA adds to the durability treatment. The purpose of this study was to describe the outcomes of single-vessel vs two-vessel mesenteric stent placement in patients with CMI secondary to atherosclerotic disease. The authors reviewed 101 patients (41 men, mean age 73 ± 13 years) who were treated with mesenteric artery stents from 1998 to 2008. Patients treated with single-vessel SMA stents (group A), two-vessel celiac artery and SMA stents (group B), and patients treated with isolated celiac artery stenting (group C), were reviewed with respect to clinical data and outcomes. The groups were analyzed for differences in morbidity and mortality and freedom from recurrent symptoms and reintervention. There were 61 patients in group A, 24 in group B, and 16 in group C. Demographics, cardiovascular risk factors, and clinical presentation were similar among the three groups. The three groups had similar early mortality (2%, 4%, and 0%, respectively), morbidity (18%, 26%, and 12%, respectively), and symptom relief (95%, 78%, and 100%, respectively). Freedom from reintervention at 1 and 3 years was similar in group A (86% ± 5% and 50% ± 9%), group B (67% ± 11% and 67% ± 11%), and group C (63% ± 13% and 63% ± 113%). Differences in freedom from restenosis were similar at 1 and 3 years in group A (54% ± 7% and 44% ± 9%), group B (47% ± 12% and 39% ± 12%), and group C (43% ± 13% and 34 ± 13%). Primary and secondary patencies at 3 years were 57% and 96% for SMA stents and 61% and 87%, respectively, for celiac stents ($P >$ .05). Celiac artery stenting alone was associated with symptom recurrence in 38% compared with recurrence rates of 18% in patients who underwent SMA stent placement ($P =$ .06). Two-vessel stenting was associated with more complications (33%) compared with stenting of the SMA (18%) or celiac artery (6%) alone. The higher complication rate was due to more interprocedural complications (residual stenosis or dissection).

Comment: There was no added benefit to two-vessel stenting compared with single-vessel stenting for treatment of CMI. Long-term results were similar, with nearly identical rates of restenosis, reintervention, and symptom recurrence. Two-vessel stenting was associated with more complications. The study was limited by its retrospective design. It is possible there was a bias toward placement of two stents in patients with more symptoms or when the anatomy of the SMA was suboptimal for stenting. It is conceivable patients with poor collateralization between the celiac and SMA with significant gastric ischemic manifestations of CMI may benefit from stenting both

arteries. Overall, however, the data do not support a policy of routine stenting of the celiac and SMA for treatment of CMI.

Safety of Stenting and Endarterectomy by Symptomatic Status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST)

Silver FL, Mackey A, Clark WM, et al. and the Crest Investigators. Stroke 2011;42:675-80.

Conclusion: For the primary Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST) end point of the composite of stroke, death, and myocardial infarction, there are no significant differences between carotid artery stenting (CAS) and carotid endarterectomy (CEA) by symptomatic status. Periprocedural stroke and death rates are significantly lower for CEA in symptomatic patients. Nearly twice as many strokes occurred in asymptomatic patients with CAS vs CEA (15 vs 8), but this did not reach statistical significance.

Summary: This is a secondary analysis of CREST data. CREST investigated the safety and efficacy CAS vs CEA in patients with high-grade carotid stenosis. A symptomatic patient was defined as having had appropriate symptoms ≤180 days of randomization. The primary end point of CREST was a composite of stroke, myocardial infarction, or death within the periprocedural period or ipsilateral stroke up to 4 years. There were 1221 symptomatic and 1181 asymptomatic patients entered into CREST. For all patients, the periprocedural aggregate of stroke, myocardial infarction, and death did not differ between CAS and CEA (5.2% vs 4.5%; hazard ratio [HR], 1.18; 95% confidence interval [CI], 0.82-1.68; $P = .38$). Rates of stroke and death, however, were higher for CAS vs CEA (4.4% vs 2.3%; HR, 1.90; 95% CI, 1.21-2.98; $P = .005$). For symptomatic patients, periprocedural stroke and death rates were 7.0% ± 0.9% for CAS and 3.2% ± 0.7% for CEA (HR, 1.89; 95% CI, 1.11-3.21; $P = .02$). For asymptomatic patients, stroke and death rates were 2.5% ± 0.6% for CAS and 1.4% ± 0.5% for CEA (HR, 1.88; 95% CI, 0.75-4.42; $P = .15$). Results were better in patients aged <80 years vs those >80 years.

Comment: Every reasonable analysis of government-sponsored randomized trials continues to indicate that CEA is superior to CAS for treatment of patients with symptomatic carotid stenosis if the goal of the procedure is to prevent stroke. Very significant questions remain about the treatment of asymptomatic patients. The large majority of patients undergoing carotid intervention in the United States do so for asymptomatic carotid stenosis. And yet, we really do not know the natural history of this disease in the modern era with more advanced antiplatelet mediations, statin medications, and better blood pressure control available now than was available 20 years ago. However, these medications will only be effective if the patients take them. What is needed is a three-arm trial in asymptomatic patients with carotid artery stenosis: medical management alone vs medical management combined with CEA vs medical management combined with CAS. The anticipated number of events, the number of patients required, and the number of centers required will likely be large for such a study. However, given the demographics of carotid interventions in the United States, the potential public health and economic effect of the results of such a trial would be felt immediately.

Apolipoprotein (a) Isoforms and the Risk of Vascular Disease: A Systematic Review of 40 Studies Involving 58,000 Participants

Erqou S, Thompson A, Angelantonio D, et al. J Am Coll Cardiol 2010;55:2160-7.

Conclusion: Smaller apolipoprotein (a) (apo[a]) isoforms confer an approximately twofold higher risk of ischemic stroke or coronary heart disease than larger isoforms of apo(a).

Summary: Lipoprotein(a) (Lp[a]) is composed of a glycoprotein molecule, apo(a), and a low-density lipoprotein (LDL) particle. Apo(a) is responsible for the properties of Lp(a). (Marcovina SM et al [Am J Cardiol 1998:82:57U-66U]; McLean JW et al [Nature 1987;330:132-7]). Increased circulating Lp(a) concentration is associated with increased risk of coronary heart disease (CHD) and stroke and is independent of other conventional risk factors for vascular disease, including total cholesterol level. The overall additive risk of abnormalities of Lp(a) is only about one-quarter that seen with LDL cholesterol level (JAMA 2009;302:412-23). However, specific Lp(a) subtypes may confer higher cardiovascular risk. If that is the case, analysis for Lp(a) subtypes may be useful in the stratification of vascular risk. The authors postulated that Lp(a) particles associated with smaller rather than larger apo(a) isoforms may result in higher cardiovascular risk. They analyzed information from 40 studies published between January 1970 and June 2009 that reported an association between apo(a) isoforms and the risk of ischemic stroke or CHD. This involved 11,396 patients and 46,938 controls in 36 studies that used comparable phenotyping and analytic methods to assess apo(a) isoform size. These studies yielded a combined relative risk for CHD of 2.08 (95% confidence interval [CI], 1.67-2.58) for subjects with smaller vs larger apo(a) isoforms. There was substantial heterogeneity among the studies ($I^2 = 85\%$; 95% CI, 80%-89%). Heterogeneity was mainly explained by differences in analytical approaches and laboratory methods. Six studies of ischemic stroke used comparable phenotypic methods with a combined relative risk of 2.14 (95% CI, 1.85-2.97).

Comment: Apo(a) size heterogeneity is a function of a copy number variation of one protein domain, kringle IV type 2, the gene for which exists in 5 to 50 identically repeated copies. Copy number variation of the gene confers marked heterogeneity in the molecular mass of the apo(a) isoform (Boffa MB [Clin Biochem 2004;37:333-43]). Apo(a) subtyping has been clinically limited because it adds a relatively modest incremental risk compared with other biomarkers for cardiovascular disease. However, this study indicates there are subtypes of apo(a) that may be worth looking for. It will need to be determined whether smaller apo(a) isoforms have sufficient relevance in determining vascular risk independent from Lp(a) concentration when compared to other more conventional risk factors for atherosclerosis.

Carotid Artery Stenting Versus Carotid Endarterectomy: A Comprehensive Meta-Analysis of Short-Term and Long-Term Outcomes

Economopoulos KP, Sergentanis TN, Tsivgoulis G, et al. Stroke 2011;42:687-92.

Conclusion: Long-term and short-term outcomes of carotid endarterectomy (CEA) are both superior to those of carotid artery stenting (CAS), but there may be subgroups where results are more equivalent.

Summary: Before this meta-analysis, the most recent meta-analysis of the results of CEA vs CAS was performed by Meier et al (BMJ 2010;340:c467). Since the Meier et al publication, there has subsequently been publication of the Carotid Revascularization Endarterectomy Versus Stent Trial (CREST), as well as publication of the long-term results of the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) and the Stent-Supported Percutaneous Angioplasty of the Carotid Artery Versus Endarterectomy (SPACE) trial. This new meta-analysis was performed to provide short-term and long-term comparisons between CEA and CAS using all available data from published randomized trials. Short-term results were defined as <30 days. Analysis and long-term outcomes were depicted with hazard ratios for >1 year results.

There were 13 randomized trials incorporating 3723 CEAs and 3754 CAS patients. CAS was associated with short-term elevated risk for stroke and "death or stroke." There was also a marginal trend towards higher death and "death or disabling stroke" with CAS. Rates of cranial nerve injury and myocardial infarction were higher with CEA. With respect to long-term results, CAS was associated with higher rates of stroke (pooled odds ratio, 1.37; 95% confidence interval, 1.13-1.65) and higher rates of "death or stroke" (pooled odds ratio, 1.25; 95% confidence interval, 1.06-1.48). Results were replicated with pooled hazard ratios. The difference in long-term stroke rates was most apparent in patients aged >68 years, with little differences observed in rates in patients aged <68 years. There was no significant heterogeneity among trials. Additional analysis did not reveal any modifying effects mediated by symptomatic or asymptomatic status, distal protection devices, early termination of trials, area of study origin, or CAS learning curve.

Comment: The frequently reported advantages of CEA over CAS in preventing short-term risk of stroke are now reported to be continued in the long-term. There are, of course, still many questions regarding the use of CEA or CAS. We do not know which is better in patients with acute stroke, nor do we know about long-term restenosis. Overall, CEA and CAS may be roughly equivalent with regard to neurologic outcome in younger patients; however, if the overall goal is to prevent stroke, CEA is more effective than CAS.

Cholesterol Efflux Capacity, High-Density Lipoprotein Function, and Atherosclerosis

Khera AV, Cuchel M, de la Llera-moya M, et al. N Engl J Med 2011;364:127-35.

Conclusion: Cholesterol efflux capacity has a strong inverse relationship with angiographic coronary artery disease and carotid intima-media thickness independent of high-density lipoprotein (HDL) cholesterol level.

Summary: A strong inverse association exists between levels of HDL cholesterol and cardiovascular disease risk. Pharmacologic increases in HDL cholesterol have thus been postulated to reduce cardiovascular risk. However, an inhibitor of cholesteryl ester transfer protein (CETP) was found to result in a 72% increase in HDL cholesterol levels, but was associated with an increase in the number of cardiovascular events (Barter PJ [N Engl J Med 2007;357:2109-22]). This may be because HDL has marked heterogeneity in particle composition that affects its biologic properties. Emphasis has therefore shifted on not only measurement of HDL cholesterol levels but on the development of a validated measure of HDL function (Vaisar T [J Clin Invest 2007;117:746-56]). There may be many components of HDL-mediated atheroprotection. The ability of HDL to promote reverse cholesterol transport by accepting cholesterol from lipid-laden macrophages may be important. This is termed "cholesterol efflux capacity" (Tall AR [J Intern Med 2008;263:256-73]).